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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/538,106	03/29/2000	Frank McKeon	HMV-038.02	7239

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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 11/20/2002

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/538,106

Applicant(s)

MCKEON F ET AL

Examiner

Christopher H Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 September 2002 ^{09/09/02}
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 1, 11, 12 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-10 and 13-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 16.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 9/3/02 (paper no. 15) is acknowledged and entered into the record. Claims 2, 4, 6 and 10 are amended, and claims 15-22 are newly added. Claim 21 is withdrawn from consideration as being drawn to a non-elected subject matter.

Therefore, claims 2-10, 13-21 are therefore examined on the record.

Information Disclosure Statement

2. The Information Disclosure Statement filed 9/9/02 (paper no.16) is acknowledged and considered. A signed copy of the IDS is attached hereto.

Specification

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

4. The disclosure is objected to because of the following informalities: There are blanks in the specification which refer to ATCC numbers.

Appropriate correction is required.

Claim Rejections Withdrawn – 35 USC § 112, 2nd paragraph

5. The rejection of claims 2-10 under 35 USC 112, 2nd paragraph as being indefinite in the recitation of the phrase “decrease in the level of said p63” is **withdrawn**, in light of the amendments set forth by the applicants.

Claim Rejections Withdrawn - 35 USC § 102

6. The rejection of claims 6-9 under 35 USC 102(a) as being anticipated by Hall *et al* is **withdrawn**, in light of the arguments set forth by the applicant.

Claim Rejections Withdrawn - 35 USC § 103

7. The rejection of claims 2-6, and 9 under 35 USC 103(a) as being obvious over Hall *et al* in view of Parsa *et al* is **withdrawn**, in light of the arguments set forth by the applicant.

New Claim Rejections - 35 USC § 112, 2nd paragraph

8. Claims 2-10, 15-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Regarding claim 2, 6, 10, and 15-22 in the recitation of the term "gene product", it is not clear as to which gene product is being referred. Applicant has elected the gene product to be a protein, however, one of skill in the art could interpret gene product to mean either nucleic acid molecule or protein. LS 1C

10. Regarding claims 15, 17, and 20 in the recitation of "TAap63 α , TAp63 β , TAp63 γ , Δ Np63 α , Δ Np63 β , Δ Np63 γ ", these are label term which have no meaning to one of skill in the art, applicant must associate specific sequence identification numbers to each of these clones so that one of skill would be able to fully understand the sequence and meaning of these terms. LS 1C

11. Regarding claims 2-10 in the recitation of "determining", it is unclear how this determination is being made (i.e. is the determination made through the addition of some reagent?). As such the metes and bounds of the term cannot be fully understood. Furthermore, it is unclear as to how the determination is made between steps (b) and LS 1C

(c), is this determination made by examination or by another type of "determination" method.

12. Regarding claims 5, 16, and 19, in the recitation of the term "RT-PCR", it is unclear how this technique is used to detect or determine the protein levels of p63. It is noted that the applicant has selected a method wherein protein levels are determined, *OR* therefore, the claims have been examined to the extent that they read of "immunoassays" only.

New Claim Rejections - 35 USC § 112, 1st paragraph

13. Claims 2-10 and 13-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting malignant carcinoma comprising determining the level of p63 protein by an anti-p63 antibody and compared to p63 concentrations of healthy cell or non-malignant cells, does not reasonably provide enablement for a method of detecting malignant carcinoma *OIC* comprising determining the level of p63 gene product in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The

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courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The nature of the invention: The claims of the instant invention are drawn to a method of detecting malignant carcinoma, detecting cancer in tissue containing sub-columnar reserve cells, distinguishing between cervical squamous carcinoma from cervical small cell undifferentiated carcinoma, and distinguishing benign prostate lesions from malignant prostate lesions comprising the determination of p63 gene product.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that p63 is a mutated isoform of the p53 cancer related gene. The art also teaches that the p63 gene has been associated with cancer (see Li *et al*/ Zhonghua Zhongliu Zazhi 1994; 16(3):172-176).

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The amount of direction or guidance present and the presence or absence of working

examples: The examples of the instant specification is drawn to the detection of the p63 gene by means of an antibody based assays, such as immunohistochemistry or immunoblotting. No where in the specification does it teach to one of skill in the art how to determine a cancerous condition from the measurement of p63 nucleic acid molecules. The specification has only taught the use of specific antibodies to p63 in the detection of cancerous conditions. There are many factors that determine the presence of a malignant or cancerous lesion from nucleic acid determination. Such factors include the development of primers that are universal to all patients in the detection of p63 and the determination of what levels of expression constitute a cancerous condition.

The breadth of the claims and the quantity of experimentation needed: Because there is a lack of clear guidance to one of skill in the art in terms of the methods used to determine the level of gene product, except for the protein levels, one of skill in the art would be forced into undue experimentation to determine how and what quantities of gene products are considered cancerous.

New Claim Rejections - 35 USC § 102

14. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

15. Claims 2-7, 9 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Pujol *et al* (Proc Amer Ass of Cancer Res Ann Meeting 1994; 35(0):165) Claims are drawn to a method of detecting malignant carcinoma comprising the determination of

no

p63 gene product (protein), wherein the malignant carcinoma is from the breast, wherein the control sample is epithelial cells, and wherein the method of determination is by immunoblotting. Claims are further drawn to a kit comprising an antibody against p63. Pujol *et al* teach a method of determining malignant carcinoma from breast when compared to control samples found in epithelium. Claims 6-7, and 9 are rejected because although not explicitly recited, breast cells are considered sub columnar cells. Inherently, the antibody used would be part of a kit and therefore anticipates claim 13.

New Claim Rejection - 35 USC § 103

16. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

17. Claims 2-7, 9, 13, 16, and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pujol *et al* (see above for Pujol *et al* teaching). Claims are directed to a method of detecting malignant carcinoma, detecting cancer in tissue containing sub-columnar reserve tissue, distinguishing cervical squamous carcinoma from cervical small cell undifferentiated carcinoma, and distinguishing benign prostate lesions from malignant prostate lesions, comprising the determination of p63 gene product in patent samples.

It would have been *prima facie* obvious to one of ordinary skill in the art to determine the p63 levels in patient tissue samples to determine the existence or presence of a malignant condition because Pujol *et al* taught the utilization of p63 as a marker for a malignant condition in epithelial derived cells. One of ordinary skill in the

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art would have been motivated to use p63 for determining a malignant condition because it is readily known in the art that carcinomas are derived from epithelial cells, and the method as taught by Pujol *et al* describe the determination of malignant conditions in a epithelial derived cell type. One of ordinary skill would have expected a reasonable amount of success in determining malignant conditions using p63 because it is taught that p63 is present in at least one type of malignant carcinoma, when compared to normal epithelial cells.

Conclusion

16. No claim is allowed. Because of the newly cited rejections made in the instant office action, the action is made **NON-FINAL**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

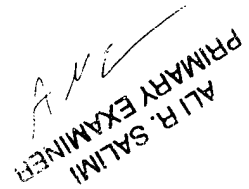
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

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A handwritten signature in black ink, appearing to read "Christopher Yaen", followed by a long horizontal line.

Christopher Yaen
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November 17, 2002

A handwritten signature in black ink, appearing to read "Ali R. Salimi", followed by a long horizontal line. Below the signature is a rectangular stamp with the text "ALI R. SALIMI" and "PRIMARY EXAMINER" in a bold, sans-serif font.